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EXAMINER	
KUBELIK, ANNE R	
ART UNIT	**PAPER NUMBER**
1638	3

DATE MAILED: 08/27/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application N .	Applicant(s)	
	10/046,769	BROWN, GREGORY G.	
	Examiner	Art Unit	
	Anne R. Kubelik	1638	

-- The MAILING DATE of this c mmunicati n appears on the c ver sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____ .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 1-4 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) 1-4 is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *with the application* is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☒ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 12 .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

1. Claims 1-4 are pending.

2. The claim for priority in the first paragraph of the instant application is incorrect. Parent application 09/447,303 was a national stage entry of PCT/CA98/00522, not a continuation of that application. Additionally it is that PCT application that claims priority to provisional application 60/047,795. Correction is required.

Claim Rejections - 35 USC § 112

3. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Claims 1-4 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method for restoring male fertility to a male sterile *pol Brassica napus* plant by transformation with an edited form of the *B. napus* atp6 gene operably linked to a stamen-specific promoter, does not reasonably provide enablement for a method for restoring male fertility to any cytoplasmically male sterile plant by transformation with an edited form of any mitochondrial gene or a method for restoring male fertility to a male sterile *pol Brassica napus* plant by transformation with an edited form of the *B. napus* atp6 gene, wherein no promoter is present or wherein the promoter is constitutive. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

The claims are broadly drawn to a method for restoring male fertility to any cytoplasmically male sterile plant by transformation with an edited form of any mitochondrial gene, wherein the gene is co-transcribed with an "unusual" CMS-associated mitochondrial gene.

The instant specification, however, only provides guidance for generation of constructs encoding edited (A6e) or unedited (A6u) atp6 or unedited orf224 (ORFu) operatively linked to mitochondrial targeting sequences and a constitutive promoter and transformation of the constructs into male sterile and male fertile *Brassica* plants; A6u made wild-type *Brassica* into partially male sterile, while A6e made sterile *pol Brassica* partially male fertile, however no seed was produced from any of these plants (pg 12-15). Seed could only be produced when a promoter that drives expression early in stamen development (AP3) was used (pg 12-14 and 16).

The instant specification fails to provide guidance for other edited forms of mitochondrial genes, wherein the gene is co-transcribed with an "unusual" CMS-associated mitochondrial gene. The instant specification fails to provide guidance for a method for restoring male fertility to any cytoplasmically male sterile plant by transformation with an edited form of any mitochondrial gene or a method for restoring male fertility to a male sterile *pol Brassica napus* plant by transformation with an edited form of the *B. napus* atp6 gene, wherein no promoter is present or wherein the promoter is constitutive.

The instant specification shows that the effect of promoter choice on the alteration of male fertility is unpredictable. Unexpected results were obtained using constructs with a constitutive promoter (*mas2'*) that were presumably not seen when an early-flower development promoter (AP3) was used. For example, Applicant was unable to obtain seeds from Westar *nap* plants made partly male-sterile by transformation with the *mas2'*/A9-A6u construct (pg. 13, lines

1-7, of the specification) and was unable to regenerate into plants transformants containing a *mas2'*/A9-orf224u (unedited orf224) construct (pg 12, lines 26-28, of the specification). The instant application states "the reduction in female fertility and other abnormalities result from the generalized expression of the fusion protein from the *mas2'* promoter" (pg 19, lines 7-10, of the specification).

Given that the claims do not specify the use of a promoter, given the unpredictability of the use of any randomly chosen promoter, given that only one edited form of any mitochondrial gene, wherein the gene is co-transcribed with an "unusual" CMS-associated mitochondrial gene is taught, and given the nature of the invention, undue experimentation would have been required by one skilled in the art to develop and evaluate methods for enhancing cytoplasmic male sterility in any plant using an unedited *atp6* or using an *orf224* gene from *B. napus* under the control of any non-exemplified or constitutive promoter.

Given the claim breath, unpredictability, and lack of guidance in the specification as discussed above, the instant invention is not enabled throughout the full scope of the claims.

5. Claims 1-3 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter that was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims are broadly drawn to a method for restoring male fertility to any cytoplasmically male sterile plant by transformation with an edited form of any mitochondrial gene, wherein the gene is co-transcribed with an "unusual" CMS-associated mitochondrial gene.

In contrast, the specification only describes a method for restoring male fertility to cytoplasmically male sterile *Brassica napus* plant by transformation with an edited form of the *B. napus atp6* gene. Applicant does not describe other DNA molecules used in the methods, and the structural features that distinguish all such nucleic acids from other nucleic acids are not provided.

Furthermore, no description is provided as to the functions of the proteins encoded by the edited form of the mitochondrial gene or the "unusual" CMS-associated mitochondrial gene.

Because the sequences are not described within the full scope of the claims, the method of using the sequences to restore male fertility to any cytoplasmically male sterile plant is likewise not described within the full scope of the claims, and the specification fails to provide an adequate written description of the claimed invention.

Therefore, given the lack of written description in the specification with regard to the structural and physical characteristics of the compositions used in the claimed methods, it is not clear that Applicant was in possession of the genus claimed at the time this application was filed.

See *Univ. of California v. Eli Lilly*, 119 F.3d 1559, 43 USPQ 2d 1398 (Fed. Cir. 1997):

> The name cDNA is not in itself a written description of that DNA; it conveys no distinguishing information concerning its identity. While the example provides a process for obtaining human insulin-encoding cDNA, there is no further information in the patent pertaining to that cDNA's relevant structural or physical characteristics; in other words, it thus does not describe human insulin cDNA .... Accordingly, the specification does not provide a written description of the invention ....

and at pg 1406:

> a generic statement such as "vertebrate insulin cDNA" or "mammalian insulin cDNA," without more, is not an adequate written description of the genus because it does not distinguish the genus from others, except by function. It does not specifically define any of the genes that fall within its definition. It does not define any structural features commonly possessed by members of the genus that distinguish them from others. One skilled in the art therefore cannot, as one can do with a fully described genus, visualize or recognize the identity of the members of the genus. A definition by function, as we have previously indicted, does not suffice to define the genus because it is only an indication of what the genes does, not what it is.

> ... A description of a genus of cDNAs may be achieved by means of a recitation of a representative number of cDNAs, defined by nucleotide sequence, falling within the scope of the genus or of a recitation of structural features common to the members of the genus, which features constitute a substantial portion of the genus. ... the claimed genera of vertebrate and mammal cDNA are not described by the general language of the '525 patent's written description supported only by the specific nucleotide sequence of rat insulin.

See *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ 2d 1016 at page 1021:

> A gene is a chemical compound, albeit a complex one, and ... conception of a chemical compound requires that the inventor be able to define it so as to distinguish it from other materials .... Conception does not occur unless one has a mental picture of the structure of the chemical or is able to define it by its method of preparation, its physical or chemical properties, or whatever characteristics sufficiently distinguish it. It is not sufficient to define it solely by it principal biological property, *e.g.*, encoding human erythropoietin, because an alleged conception having no more specificity than that is simply a wish to know the identity of any material with that biological property.

6. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

7. Claims 1-4 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Dependent claims are included in all rejections.

In claims 1 and 4, part (a), it is not clear if the plant cell into which the construct is introduced is from a male sterile plant or a male fertile one.

Claim 1 is indefinite in the recitation of "an edited form of a normal mitochondrial gene". Genes are not edited; RNA gene products are.

Claim 1 is indefinite in the recitation of "unusual CMS-associated mitochondrial gene". The manner in which the gene is unusual is unclear - unusual compared to what?

It is unclear in claim 3 how selecting for plant cells that have acquired the gene construct of step a is effected using a plant transformation vector. Should "b)" be replaced with --a)--?

Claim 4 is indefinite in the recitation of "unedited form of an atp6 gene of *Brassica napus*." Genes are not edited; RNA gene products are. Additionally, does *Brassica napus* have more than one atp6 gene?

8. Claims 1-4 are rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting an essential element, such omission amounting to a gap between the elements. See MPEP § 2172.01. The omitted element is a promoter for expression of the genes. The instant specification emphasizes the need for a specific type of promoter: "the data also indicate that do *[sic]* avoid deleterious effects on vegetative growth and female fertility, it is necessary to express these constructs using a tissue specific or inducible promoter" (pg 19, lines 20-24), given the stated goal of enhancing cytoplasmic male-sterility for use in hybrid crop production in crops like canola where the harvested product is the seed (pg 5 lines, 13-16, and pg 3, line 25-27). It is suggested that the claims be modified to incorporate this element and that the promoter be one that developmentally targets the expression of the construct to relevant tissues.

9. Claims 1-4 are free of the prior art. The closest prior art is that of Zabaleta et al (1996, Proc. Natl. Acad. Sci. USA 93:11259-11263), who teach a method for restoring male fertility to a cytoplasmically male sterile tobacco plant by introduction of an unedited form of the wheat atp9 mitochondrial gene into the plant; the gene is in an antisense orientation. The male sterile plant had been transformed with the sense version of the unedited form of the wheat atp9 mitochondrial gene, and the gene was introduced into it by crossing with a plant transformed with the antisense version of the unedited form of the wheat atp9 mitochondrial gene (Figure 1, pg11261, left column, paragraph 3).

Conclusion

10. No claim is allowed.

11. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Anne R. Kubelik, whose telephone number is (703) 308-5059. The examiner can normally be reached Monday through Friday, 8:30 am - 5:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Amy Nelson, can be reached at (703) 306-3218. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 872-9306 for regular communications and (703) 872-9307 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to Customer Service at (703) 308-0198.

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August 14, 2003

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